UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/812,393	03/05/1997	LINDA A. SHERMAN	313332000100	2284

21874 7590 07/07/2005

EDWARDS & ANGELL, LLP
P.O. BOX 55874
BOSTON, MA 02205

EXAMINER	
WILSON, MICHAEL C	
ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 07/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/812,393	SHERMAN ET AL.	
	Examiner	Art Unit	
	Michael C. Wilson	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 February 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4,5 and 22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,5 and 22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 3 and 6-21 have been canceled. Claims 1, 2, 4, 5 and 22 remain pending and are under consideration in the instant office action.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Applicant's arguments filed 5-2-05 have been fully considered but they are not persuasive.

Claim Objections

The objection to claim 1, step a), regarding the production of human HLA restricted CTL has been withdrawn in view of the amendment.

Claim Rejections - 35 USC ' 112

The rejection of claims 1, 2, 4, 5 and 22 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement has been withdrawn in view of the amendment.

The limitation of "a single-chain T cell receptor comprising a variable region of a mouse TCR α chain fused to a variable region of a mouse TCR β chain, said TCR α and TCR β chains comprising a mouse TCR, wherein the single-chain TCR is specific for a tumor-associated antigen (TAA) and restricted by human HLA" in claim 1 has support on page 3, lines 2-22; on page 4, lines 1-4; on page 5, line 25; on page 6, lines 1-7; on page 7, lines 4-10 and 24-25; from page 8, line 25, to page 11, line 4; from page 12, line

10, to page 13, line 2; on page 13, lines 11-18; and in the Examples, particularly in Examples 1-3, and Figures, as originally filed.

Support for step a) is found on pg 3, lines 13-18 (see citation above).

Support for step b) is found in Example 3, for example.

Support for steps c) and d) is found on pg 12, lines 10-15, and pg 13, lines 1-2. The resulting nucleic acid sequences of the α and β TCR variable regions amplified and recovered are shown in Fig. 7A and 7B.

Support for fusing the TCR α chain and β chain step to make a single chain TCR comprising a variable region of the TCR α chain fused to a variable region of the TCR β chain in step e) is found on pg 6, lines 16-18 ("Similarly, in Figure 1, construction of a single chain TCR wherein the variable regions of the α and β chains are fused through a linker and then fused to the ζ region is shown with and without the CD8 hinge").

The phrase "single chain TCR of step e comprises a TCR derivative comprising a TCR α chain and TCR β chain, wherein the TCR derivative retains the HLA human restriction and TAA-specificity characteristics of the TCR of step a" in claim 22 as newly amended has support on pg 5, lines 23-25 ("The recombinant materials relevant to the invention include those associated with the TCR produced by the nonhuman subject per se, and also derivatives of this TCR which retain their HLA restriction and specificity characteristics").

The rejection of claims 1, 2, 4, 5 and 22 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for obtaining mouse TCRs and

immunizing transgenic mice that express human HLA molecules, does not reasonably provide enablement for obtaining any species of TCR other than mouse or immunizing any transgenic non-human mammal species having human HLA as broadly claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims has been withdrawn because the methods have been limited to immunizing transgenic mice that produce human HLA and isolating mice TCRs.

Claims 1, 2, 4, 5 and 22 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention in part for reasons of record.

The preamble of claim 1 as newly amended remains indefinite because it is not commensurate in scope of the body of the claim. The preamble requires the production of a nucleic acid fusion molecule while step e requires fusing the recovered TCR α chain nucleic acid product to the recovered TCR β chain nucleic acid product "to prepare the isolated fused nucleic acid molecule...." The fusion of the TCR α and β chains in step e should result in "preparing an isolated fused nucleic acid molecule..." as in the preamble of the claim. Replacing "to prepare the isolated fused nucleic acid molecule... ...restricted" with "thereby preparing an isolated fused nucleic acid molecule... ...restricted" would overcome this rejection. Upon making the suggested amendment to step e, the phrase "having a nucleotide sequence encoding... ...restricted by human HLA" in the preamble can be deleted because the body of the

claim sets forth the requirements of the "isolated nucleic acid fusion molecule." If applicants decide not to make the suggested amendment to step e, the language used to describe the "isolated nucleic acid fusion molecule" in the preamble should exactly match the language used to describe the "isolated nucleic acid fusion molecule" in step e. For example, "restricted by human HLA" in the preamble does not correlate to "human HLA restricted" in step e as currently written.

The phrase "said TCR α and TCR β chains comprising a mouse TCR" in the preamble of claim 1 as newly amended is indefinite. It cannot be determined how the phrase is intended to further limit the TCR α and β chains, which are already limited to variable regions of a mouse TCR α or β chain.

The preamble of claim 1 is indefinite because the first use of the phrase "T-cell receptor" does not have the abbreviation "(TCR)" after it in parentheses, thus making the first use of "TCR" ambiguous.

Claim 1 as newly amended is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The preamble requires isolating a single chain TCR comprising a variable α β chain, wherein the single chain TCR is specific for a TAA and is restricted by human HLA. However, the claim merely requires injecting a transgenic mouse that expresses human HLA with TAA and isolating their CTL. The claim does not require any step in which variable TCR α and β chains that recognize the TAA or a single chain TCR that recognizes the TAA are selected. Without the step, it is not readily apparent that any TCR isolated from CTL recovered from mice injected with

a TAA would recognize the TAA as claimed. Therefore, the step required to select single chain TCRs, or individual variable α or β chains that recognize the TAA has been omitted.

Claim 1, step a, remains indefinite for reasons of record. It is unclear if the CTL has i) a single chain TCR comprising a mouse TCR α chain and a mouse TCR β chain, wherein said single chain TCR is specific for said TAA or ii) a single TCR comprising a mouse TCR α chain that is specific for said TAA and a mouse TCR β chain that is specific for said TAA. Applicants have not addressed this rejection

Claim 1, step e, remains indefinite in view of the preamble for reasons of record. It is unclear whether the single-chain fusion protein as a whole is specific for said TAA or if both the variable TCR α chain and the variable TCR β chain used to make the single-chain fusion protein are specific for TAA. Applicants have not addressed this rejection.

Claim 22 remains indefinite for reasons of record. The metes and bounds of a single chain TCR comprising a TCR "comprising a TCR α chain and a TCR β chain, wherein the TCR derivative retains the human HLA restriction and TAA-specificity characteristics of the TCR of step a)" cannot be determined. It is unclear if the single chain have an α chain and a β chain, both of which are human HLA restricted and TAA-specific (a narrower scope) or the if the claim is meant to encompass any single chain TCR with a TCR α chain and TCR β chain that is human HLA restricted and TAA-specific (a broader scope). It cannot be determined if the "TCR α chain and TCR β

chain" in step e refer to the mouse TCR α and β chains in the preamble or if "the TCR α chain and TCR β chain" refer to specific TCRs in item ii) of step a) that recognize TAA.

The prior art of record does not teach or suggest immunizing mice with TAA, obtaining CTL from the mice, cloning their variable TCR α and β chains and fusing a nucleic acid sequence encoding a variable TCR α chain with a nucleic acid sequence encoding a variable β chain such that a nucleic acid sequence encoding a single-chain TCR that recognizes the TAA is obtained. Change (1994, PNAS, Vol. 91, pg 11408-11412) and WO 95/06409 submitted in the IDS filed 11-24-04 have been reviewed in particular.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

No claim is allowed.

Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached at the office on Monday, Tuesday, Thursday and Friday from 9:30 am to 6:00 pm at 571-272-0738.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

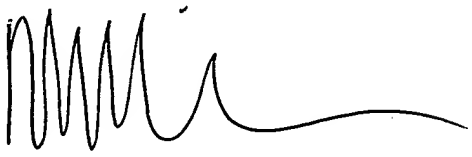
Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on 571-272-0735.

The official fax number for this Group is (571) 273-8300.

Michael C. Wilson



MICHAEL WILSON
PRIMARY EXAMINER